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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/705,940	FIKE, RICHARD M.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,15,16,22-29,31-34 and 36-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,15,16,22-29,31-34 and 36-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed August 16, 2005. Amendments were made to the claims.

Claims 1-10, 15, 16, 22-29, 31-34 and 36-44 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, mailed February 17, 2005, that is not addressed in this action has been withdrawn.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 6-8, 10, 15, 16, 22-29, 31-34, 36-41 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by SIGMA catalog 1994 (see entire document; henceforth SIGMA).

SIGMA teaches the construction of several powdered media formulas, including BGJ_b medium (see the top of the left column of page 13) and F-12 Coon's Modification medium (see for example the bottom of the right column of page 15). The formulations/methods for making these media are presented on pages 217 and 221 of SIGMA, respectively.

In the case of BGJ_b medium, the ratio of sodium phosphate dibasic and sodium phosphate monobasic salts are determined to give a pH of 6.2 upon reconstitution (see the formulation on

page 217). The medium also includes several addition components, including D-glucose (carbon source), vitamins and other culture medium supplements (see the formulation on page 217). The powdered medium can be reconstituted in a solvent such as water. Importantly, the culture medium is capable of supporting the growth of eukaryotic cells, such as embryonic cartilaginous bone cells (see the introductory paragraph at the top of the page); this also represents a method for culturing eukaryotic host cells using the reconstituted BGJ_b medium. Furthermore, absent evidence to the contrary and given that the medium contains all components that are capable of supporting the growth of a yeast cell (such as a carbon source and nitrogen source), and given the propensity of microorganisms to contaminate cell culture systems, this medium is also capable of supporting the growth of yeast cells.

In the case of F-12 Coon's Modification medium, the ratio of sodium phosphate dibasic and potassium phosphate monobasic salts are determined to give a pH of 5.7 upon reconstitution (see the formulation on page 217). The medium also includes several addition components, including D-glucose (carbon source), vitamins and other culture medium supplements (see the formulation on page 217). The powdered medium can be reconstituted in a solvent such as water. Importantly, the culture medium is capable of supporting the growth of eukaryotic cells, such as hybrid cells produced by viral fusion (see the introductory paragraph at the top of the page); this also represents a method for culturing eukaryotic host cells using the reconstituted F-12 Coon's Modification medium. Furthermore, absent evidence to the contrary and given that the medium contains all components that are capable of supporting the growth of a yeast cell (such as a carbon source and nitrogen source), and given the propensity of microorganisms to

contaminate cell culture systems, this medium is also capable of supporting the growth of yeast cells.

Note- additional pages that are not cited specifically above are included with the SIGMA reference as a demonstration that SIGMA teaches further methods for producing automatically pH-adjusting powdered medium comprising a specific ratio of mono- and dibasic-phosphate salts.

Claims 1, 2, 5, 6, 8, 10, 15, 16, 28, 29, 31-34, 36, 40 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Fluka catalog 1995/1996 (see entire document; henceforth Fluka). Note- this rejection is essentially the same as the previous rejection under 35 USC 102(b) regarding Fluka Cat. No. 86494, but is made in view of the current reference in order to satisfy Applicant's argument that the previous reference does not have a proper 102(b) date.

Fluka teaches a medium preparation that comprises pH-opposing forms of buffer salts, namely K_2HPO_4 and KH_2PO_4 (see for example the "Ingredients" section of Fluka). Prior to reconstitution, the medium preparation represents a dry powdered medium that produces a desired final pH upon reconstitution, and the recipe represents a method of making the dry medium. Upon reconstitution of the powder, the medium gives a pH that is desired because the medium is conducive for the growth of bacterial cells, given the "Starter Culture" method disclosed under the "Directions" section of the disclosure. Thus, Fluka also teaches a method of reconstituting the dry powdered culture medium into a liquid culture, followed by a method of growing bacterial cells such as *E. coli* in the reconstituted culture medium (see for example the "Directions" section). Upon the incubation of the bacterial cells in the presence of the culture

medium, Fluka teaches a composition comprising the culture medium and at least one bacterial cell. Since the kits as claimed are defined by the components therein, they are anticipated by the teaching of the medium composition; importantly, the culture medium also comprises other culture medium supplements, such as Yeast Extract and glycerol. Finally, although Fluka teaches the intended use of this medium for the growth of bacterial (prokaryotic) cells, the medium comprises all of the ingredients necessary for growing eukaryotic cells such as yeast, absent some evidence indicating that yeast cells can never grow in this medium.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5, 6-8, 10, 15, 16, 22-29, 31-34, 36-41,44 and 3*, 4*, 9*, 42* and 43* are rejected under 35 U.S.C. 103(a) as being unpatentable over SIGMA (as recited above in the rejection of claims 1, 2, 5, 6-8, 10, 15, 16, 22-29, 31-34, 36-41 and 44 under 35 USC 102(b)) in view of WO 98/36051 (as recited in previous Office Actions, see entire document, henceforth Fike). Note- "*" indicates those claims that are rejected specifically by the combination of references.

SIGMA teaches all of the elements set forth above. Briefly, SIGMA teaches the construction of powdered culture media capable of supporting the growth of various eukaryotic cells upon reconstitution in a solvent such as water. Importantly, the construction of the various

media set forth in SIGMA involve the determination of a ratio between monobasic and dibasic phosphate salts which give a desired pH upon reconstitution of the powder. However, SIGMA does not specifically teach: (a) the sterilization of the powder medium, (b) the use of non-CO_2 liberating sodium bicarbonate or (c) the supplementation of the medium with serum.

Fike teaches a method for producing nutritive media comprising media supplements and buffers in a dry powder, followed by sterilization of the powder with gamma-rays and packaging of the powder (see for example page 6, lines 9-19). The media can be bacterial media, yeast media, plant culture media or animal cell culture media (see for example page 6, lines 21-23). Supplements for the media include powdered sera from animals, plants, etc., cytokines and growth factors, other proteins, vitamins, amino acids, co-factors, lipids, extracts of animal tissues or glands, and buffers (see for example page 6, line 25 to page 7, line 26). Upon reconstitution of the dry powder in a solvent of interest, the media automatically adjusts to a particular pH without the use of a pH-adjusting agent such as an acid or a base (see for example page 20, lines 3-26). Fike also teaches methods of using the media to culture cells (bacteria, yeast, animal, etc.), comprising reconstituting the media compositions of the above method in a solvent such as water or serum, and contacting cells with the solution under conditions that are favorable for growth of the cell (see for example page 8, lines 22-26). Fike also teaches kits for use in the above process of culturing cells comprising packaging the media, and in some embodiments including the dried cells for culturing (see for example page 8, lines 6-11). Fike must have used sodium bicarbonate that does not liberate CO_2 because the invention as taught by Fike could not be practiced if carbon dioxide was liberated in the packaged media. The accumulation of carbon dioxide in an enclosed package would result in a build up of pressure, eventually leading to an

explosion of the container, thereby comprising the sterility of the dry powder and counteracting a distinct step in the process as taught by Fike. Fike further requires that the powdered media be sterilized by gamma irradiation.

It would have been obvious to combine the teachings of SIGMA with those of Fike because each teaching concerns the preparation of medium that has a desired pH upon reconstitution. Furthermore, SIGMA teaches a method of obtaining a desired pH without using extraneous pH-adjusting agents such as HCl or NaOH; this is in accordance with the suggestion in Fike that extraneous pH-adjusting agents be omitted from the media preparations. The ordinary skilled artisan would have been motivated to combine the teachings of SIGMA and Fike because SIGMA teaches that the use of appropriate concentration of pH-opposing salts is a well-known and accepted manner of maintaining the pH of culture medium, while at the same time meeting the suggestion of Fike to not use additional pH-adjusting agents. Absent evidence to the contrary, the ordinary skilled artisan would have had a reasonable expectation of success when practicing the claimed invention given the combined teachings of SIGMA and Fike.

Claims 1, 2, 5, 6, 8, 10, 15, 16, 28, 29, 31-34, 36, 40, 41 and 3*, 4*, 7*, 9*, 22-27*, 37-39*, and 42-44* are rejected under 35 U.S.C. 103(a) as being unpatentable over Fluka (as recited above in the rejection of claims 1, 2, 5, 6, 8, 10, 15, 16, 28, 29, 31-34, 36, 40 and 41 under 35 USC 102(b)) in view of Fike (as recited above and in previous Office Actions). Note- "*" indicates those claims that are rejected specifically by the combination of references.

Fike teaches a method for producing nutritive media comprising media supplements and buffers in a dry powder, followed by sterilization of the powder with gamma-rays and packaging

of the powder (see for example page 6, lines 9-19). The media can be bacterial media, yeast media, plant culture media or animal cell culture media (see for example page 6, lines 21-23). Supplements for the media include powdered sera from animals, plants, etc., cytokines and growth factors, other proteins, vitamins, amino acids, co-factors, lipids, extracts of animal tissues or glands, and buffers (see for example page 6, line 25 to page 7, line 26). Upon reconstitution of the dry powder in a solvent of interest, the media automatically adjusts to a particular pH without the use of a pH-adjusting agent such as an acid or a base (see for example page 20, lines 3-26). Fike also teaches methods of using the media to culture cells (bacteria, yeast, animal, etc.), comprising reconstituting the media compositions of the above method in a solvent such as water or serum, and contacting cells with the solution under conditions that are favorable for growth of the cell (see for example page 8, lines 22-26). Particular cells that can be used in the method are animal/human cells, including normal, transformed diseased, etc. cells (see for example page 8, line 22 to page 9, line 5). Fike also teaches kits for use in the above process of culturing cells comprising packaging the media, and in some embodiments including the dried cells for culturing (see for example page 8, lines 6-11). Fike must have used sodium bicarbonate that does not liberate CO_2 because the invention as taught by Fike could not be practiced if carbon dioxide was liberated in the packaged media. Fike requires that the powdered media be sterilized by gamma irradiation. The accumulation of carbon dioxide in an enclosed package would result in a build up of pressure, eventually leading to an explosion of the container, thereby comprising the sterility of the dry powder and counteracting a distinct step in the process as taught by Fike.

Fike does not specifically teach using pH-opposing forms of buffer salts to maintain the pH of the medium at a desired level. Rather, Fike teaches using a pH-adjusting agent such as HCl or NaOH in the dry powder to obtain a desired pH upon reconstitution of the dry powder. However, Fike clearly suggests that the media automatically adjust to a particular pH without the further use of an adjusting agent (see for example page 20, lines 3-26).

Fluka teaches a media preparation that comprises pH-opposing forms of buffer salts, wherein the pH-opposing forms of the medium are present to buffer the medium against a drop in pH (see for example the "Ingredients" and "Directions" sections of Fluka). This represents an alternative mechanism of obtaining a desired pH upon the reconstitution of a dry powdered medium, without the need for pH-adjusting agents such as HCl and NaOH. Fluka also teaches reconstituting the medium preparation containing a given cell, methods of culturing the cell in the reconstituted medium, as well as kits and compositions thereof. Buffers that would satisfy this requirement are well known in the art, and include buffer salts such as sodium phosphate (mono- and dibasic), potassium phosphate (mono- and dibasic), sodium bicarbonate (mono- and dibasic), etc.

It would have been obvious to combine the teachings of Fluka with those of Fike because each teaching concerns the preparation of medium that has a desired pH upon reconstitution. Furthermore, Fluka teaches a method of obtaining a desired pH without using extraneous pH-adjusting agents such as HCl or NaOH; this is in accordance with the suggestion in Fike that extraneous pH-adjusting agents be omitted from the media preparations. The ordinary skilled artisan would have been motivated to combine the teachings of Fluka and Fike because Fluka teaches that the use of appropriate concentration of pH-opposing salts is a well-known and

accepted manner of maintaining the pH of culture medium, while at the same time meeting the suggestion of Fike to not use additional pH-adjusting agents. Absent evidence to the contrary, the ordinary skilled artisan would have had a reasonable expectation of success when practicing the claimed invention given the combined teachings of Fluka and Fike.

Response to Arguments Concerning the Previous Rejections As They Regard the Instant Rejections

Although the rejections set forth above are technically "new rejections," applicant's arguments will be addressed regarding the use of the Fluka 1995/1996 catalog above, as said rejections are substantially the same as the previous rejection concerning the use of Fluka Cat. No. 86494. The following arguments are presented in regard to the previous rejections under 35 USC §§ 102(b) and 103(a):

1. Applicant argues that the previous rejection using Fluka Cat. No. 86494 is improper because it does not have a proper 102(b) date, and that the Office's reference to the 1987 publication date for the preparation of Terrific Broth is inconsequential to establishing the priority date for the Fluka catalog (see for example page 3 of Applicant's response).

2. Applicant argues that Fluka does not teach a eukaryotic culture broth. First, it is Applicant's position that "eukaryotic culture broth" is not an intended use of the culture medium, but rather a modifier that relates to the constitution of the medium preparation as claimed (see for example page 4 of Applicant's response). Applicant supports their contention that Fluka does not teach a eukaryotic culture broth because the addition of glycerol occurs after reconstitution of the

medium, and that no other carbon source is present in the medium composition (see for example page 5 of Applicant's response).

3. With regard to the rejection under 35 USC 103(a), Applicant suggests that the motivation to combine Fluka and Fike is not proper (see for example pages 6-7 of Applicant's response). Specifically, Applicant argues that the passage quoted by the Office to support the rejection applies only to the teachings of Fike; in other words, the desirability statements set forth in Fike are appropriate only in the context of Fike, and the ordinary skilled artisan would recognize that "there is no reason to modify this reference [Fike] or to look elsewhere for these advantages."

Applicant's arguments have been fully considered, but are not persuasive to obviate the rejection above using the "more appropriate" Fluka reference for the following reason:

1. The newly cited reference clearly demonstrates that the formulation of Terrific Broth was available and practiced more than one year prior to the earliest priority date of the instant application. Specifically, the Fluka reference provided in the instant rejection has a publication date of at least 1995/1996. As such, the teaching of Terrific Broth as presented previously and as indicated above was known prior to the instant claims.

2. Applicant first argues that the term "eukaryotic culture medium" is not an intended use. This is not convincing because there is no specific element set forth in the claim that provides a structural limitation defining a "eukaryotic culture medium" over a "non-eukaryotic culture medium." In other words, there is no limitation in the instant claims that states what makes the instantly claimed culture medium (and/or method of making said medium) patentably distinct from the culture medium taught by Fluka (Terrific Broth). Rather, the term is introduced into

the claim because it is known that Terrific Broth (henceforth TB) is *typically used* for the culturing of prokaryotic organisms, such as bacteria; i.e., the intended use of TB is not for culturing eukaryotic cells. However, this "typical use" does not mean that TB *cannot* support the growth of eukaryotic organisms, such as yeast. Indeed, contamination of TB cultures with yeast cells often occurs, yet it is not routine for laboratories to publish results indicating that their cultures were contaminated, as such cultures are generally discarded in order to obtain non-contaminated cultures. Applicant provides no evidence to the contrary of the Office's position that TB can support the growth of a yeast cell.

Applicant additionally argues that the TB contains no carbon source in its dry powdered form because the glycerol is added after reconstitution of the medium. However, it is not stated anywhere in the claims that a particular carbon source is required to define a "eukaryotic culture medium." Thus, Applicant is arguing that Fluka does not teach a limitation that is not set forth in the claims as a means of traversing the rejection, and this is not a persuasive argument.

3. Applicant's argument that the desirability for obtaining cost and time savings and reducing contamination as set forth in Fike is not applicable to the teachings of Fluka is unsubstantiated. Applicant provides no reason why the principles set forth in Fike are not applicable to the teachings of Fluka; indeed, the Office demonstrates that the teachings are directed to the same goal-a production of a powdered self-adjusting pH medium- and are obviously combinable. Additionally, it is unclear why Applicant believes Fluka would not want to combine the teachings of Fluka and Fike to save cost, save money and reduce contamination of their media. These are obvious advantages to producing any type of commercial medium, which Fluka is clearly directed to. Absent a specific reason as to why Fluka would not be motivated to produce

their medium in a time and money saving manner, as well as to produce a contamination-free medium, the motivation set forth in Fike is appropriate for combining the teachings of Fike and Fluka.

In conclusion, Applicant's arguments concerning the combination of Fluka and Fike have all been addressed, and none have been found convincing. As such, the new rejection set forth above using the properly dated Fluka reference in place of the "Fluka Cat. No. 86494" reference is found to be appropriate in view of Applicant's arguments to the contrary.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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JAMES KETTER
PRIMARY EXAMINER